Global Journal of Pure and Applied Mathematics.
ISSN 0973-1768 Volume 12, Number 1 (2016), pp. 1061-1068

http://www.ripublication.com

A Stochastic Approach to Determine Expected Time to Cross Antigenic Diversity Threshold of HIV Infected using Smallest Order Statistics

S.C. Premila[1]*, S. Srinivasa Raghavan[2]* and S. Parvarthi[3]

Mar Gregorios College of Arts & Science, Chennai–600037, India.
Veltech Dr. R.R. & Dr. S.R. Technical University, Avadi, Chennai, India.
Veltech Multitech Engineering, Avadi, Chennai, India.

Abstract

The expected time to seroconversion is a paramount aspect in the study of HIV infection and it's progression to AIDS. The antigenic diversity threshold and the expected time to cross the same due to the incrementation in antigenic diversity in successive contacts has been discussed by utilizing stochastic models by several authors. In the estimation of expected time to cross the antigenic diversity threshold, there is a consequential role for the interarrival time between successive contacts and it has a paramount influence. We propose a stochastic model under the postulation that the interarrival time between contact form most minute order statistics. In developing such a stochastic model the concept of shock model and cumulative damage process are utilized. Numerical illustration are additionally given utilizing simulated data.

Keywords: Seroconversion, Antigenic Diversity threshold, Acquired Immuno Deficiency Syndrome, Order Statistics, Human Immuno Deficiency Virus.

Introduction

The spread of HIV among the human beings is really alarming Mathematical and statistical models regarding several aspects of AIDS infection were developed and attempts are made to be apply these findings in real life situations. The use of stochastic model in the study of HIV infection transmission and spread of AIDS is quite common. The transmission of HIV occurs through different modes but the most commonly and widely prevalent mode of transmission is the homo or heterosexual contacts.

In this paper a stochastic model for the estimation of the expected time to seroconversion E(T) and it's varience V(T) is discussed. In doing so the time to seroconversion is taken to be a random variable T. It is quite natural that a person who has homo or hetero sexual contacts with an infected person continues to have successive contacts at random time intervals. Kannan etal[3, 4] have studied A stochastic approach to determine the expected time to seroconversion of HIV infected. The infected person acquires more and more of HIV in successive contacts and this contribute to what is called the antigenic diversity of the HIV. The contribution to the antigenic diversity on successive contacts and this contribute to what is called the antigenic diversity of the HIV studied by premila[7]. The contribution to the antigenic diversity on successive contacts may be interpreted as damages to the immune system. Every individual has a threshold level of antigenic diversity. If the cumulative contribution on successive contacts crosses this random level of threshold then the seroconversion takes place for a detailed study of antigenic diversity threshold and it's estimation one can refer to Nowak and May[5]. Stilanakis[8], In the present model, the shock model and cumulative process as discussed by Essay Marshall and Proschan[1] is used. In doing so, it is interpreted that at every contact the infected person receives a random amount of contribution to the antigenic diversity and when the total contribution crosses the random threshold level the seroconversion takes place. The antigenic diversity threshold is also taken to be a random variable. It may be observed that the interarrival times between successive contacts is also a random variable. A random sample 'n' of interarrival times can be taken and such values can be arranged in the increasing order of magnitude. This forms a sequence $U_{(1)} < U_{(2)} < \ldots.. < U_{(n)}$ which form an order statistics. Jewel N. P. and Shiboshi[2] Using the probability distribution of the order statistics, the present model is developed. The random variable which denotes the interarrival times between successive contacts is such that it is distributed as that of an order statistics. Parvathi[6] etal stochastic analysis of single product inventory system using Geometric distribution. In this paper it is assumed that threshold follows geometric distribution and interarrival time form an order statistics and so they are not independent. This is due to the fact that the smallest order statistics is taken, it implies that the interarrival times are becoming smaller. Hence frequent contacts would be possible which will have impact on the time to seroconversion. Numerical illustrations are provided using stimulated data.

Assumptions of the Model

- Sexual contact is the only source of HIV infection.
- An uninfected individual has sexual contacts with a HIV infected partner and every contact a random number of HIV is getting transmitted.
- The damage process of the immune system is linear and cumulative.
- Antigenic diversity is caused by transmission of HIV at each contact whose interarrival times are assumed to be identically independent random variables.
- If the total antigenic diversity exceeds threshold level y which is itself a random variable, the conversion from seronegative to seropositive status occurs and the person becomes seropositive.

- The process which generates the contacts, the sequence of damages and the threshold are mutually independent.
- From the collection of a large number of interarrival times between successive contacts of persons a random samples of 'n' observations are taken.

Notations:

X_i: A random variable denoting the amount of contribution to antigenic diversity due to the HIV transmitted in the i^{th} contact, in other words the damage caused to the immune system in the i^{th} contact with p. d. f. g(.) and c. d. f. G(.).

Y: A random variable representing antigenic diversity threshold which follows geometric distribution with parameter θ.

T: A random variable denoting the time to seroconversion.

$P_n = P(x_i = n)$, the probability that 'n' particles of HIV are transmitted during the i^{th} contact.

U_i: A random variable denoting the interarrival time between successive contacts with p. d. f. f(.) and c. d. f. F(.).

$\Phi(S) = \sum_{k=0}^{\infty} P_k S$ is the p. g. f. of X.

$V_k(t)$ = Probability of exactly k contacts in (0, t)

$\bar{\theta} = 1-\theta$.

$U_{(1)}$: a continuous random variable denoting the interarrival times between contacts follows smallest order statistics with p. d. f. $f_{u(1)}{}^{(t)}$ and c. d. f. $F_{u(1)}{}^{(t)}$.

T: the random variable representing the time to seroconversion.

$g_k(.)$: the p. d. f. of the random variable $\sum_{i=1}^{k} X_i$

$F_k(.)$: the k convolution of F(.)

Results

$S(t) = P(T > t)$

$= \sum_{k=0}^{\infty}$ Pr {there are exactly k contacts in (0, t)}

X P_r {the cumulative total of antigenic diversity < y}

$= \sum_{k=0}^{\infty} V_k(t) P(\sum_{k=0}^{\infty} X_k < y)$

Let $P(y = 1) = \theta$ represent the probability that the threshold level is equal to one. $P(y = 2) = \theta\,\bar{\theta}$ which implies that the probability the conversion takes place only when y = 2.

Similarly, $P_j = P(y = j) = \theta\,\bar{\theta}^{j-1}$

/The probability generation function is φ is

$$\Phi(S) = \sum_{k=0}^{\infty} P_k S^k = \sum_{k=1}^{\infty} \bar{\theta}^{k-1}\theta S^{k-} \qquad (5.1)$$

$S\theta \sum_{k=0}^{\infty}(S\theta)^{k-1} = \frac{-s\theta}{1-s\theta}$

$/P(X < Y) = \sum_{n=1}^{\infty} P_n{}^1 (P(y > n))$

Let $P(y > n) = \sum_{n=1}^{\infty} P(y = n+i)$

$P(y > n) = \theta^n$

$$/P(X < Y) = \sum_{n=1}^{\infty} P_n(\theta)^{\bar{n}} = \Psi(\bar{\theta}) \qquad -(5.2)$$

Which is the probability that an individual is not getting infected in a single contact. The probability that the cumulative damage has not crossed the threshold level in k contacts is equal to S_k and
$P(X_1 + X_2 + \ldots + X_k < y) = [\Psi(\theta)]^k$

Now $1-S_k = 1-[\Psi(\theta)]^k$ is the prevalence function mentioned in Jewell and Shiboski (1990).

Let F(t) be the distribution function of a random variable U_i which is the interarrival time between contacts and U_i's are i. i. d random variables having exponential distribution with parameter C.
$V_k(t) = P[U_1+U_2+\ldots+U_k<t<U_1+U_2+.. +U_{k+1}]$
P(k contacts in (0, t]) = $[F_k(t)-F_{k+1}(t)]$, where $F_k(t)$ is the distribution function of $U_1+U_2+U_3\ldots+U_k$
$S(t) = \sum_{k=0}^{\infty} V_k(t) [\Psi(\theta)]^k$
$= \sum_{k=0}^{\infty} V_k(t) [\Psi(\theta)]^k$
Let L(t) = 1-S(t)
$=[1-(\Psi(\theta))] \sum_{k=1}^{\infty}[\Psi(\theta)]^{k-1} F_k(t)$
The Laplace stieltjes transform of
L(t) is $L^*(S) = \{[1-(\Psi(\theta))] \sum_{k=1}^{\infty} \Psi(\theta)]^{k-1} f^*(s)\}$

$$= \frac{[1-\Psi(\theta)]\, f^*(s)}{[1-\Psi(\theta) f^*(s)]} \quad - \quad (5.3)$$

On simplification
The interarrival times $U_1, U_2, U_3, \ldots U_k$ are i. i. d. random variables and $U_{(1)}<U_{(2)}<\ldots.<U_{(k)}$ form k order statistics which are also random variables which are not independent. Now considering the first order statistics $u_{(1)}$ it can be shown that the p. d. f. of $U_{(1)}$ is $fu_{(1)}(t) = k[1-F(t)]^{k-1} f(t)$.
Taking the Laplace transform of t, we can
$f^*u_{(1)}(s) = \int_0^{\infty} e^{-st} k[1-F(t)]^{k-1} f(t)dt$ -(5. 4)
If f(.) ~ exp(θ)
$f^* u_{(1)}(S) = \frac{K\theta}{K\theta+S}$ -(5. 5)
From (5. 1) we have if $P_n=P(x=n) =(1/2)^n$
$/\Psi(\theta) = \sum_1^{\infty} P_n{}^1\theta^1$
$= \sum_{n=1}^{\infty}(t)^n \theta^n$
$= \frac{1-\theta}{1+\theta}$

Substituting (5. 5) in (5. 3) and it can be shown that

$$l^*(s) = \frac{(1-\Psi(\bar{\theta}))\, f^*u_1(s)}{1-\Psi(\bar{\theta})\, f^*u_1(s)}$$

$$l^*(s) = \frac{1-\left[\frac{(1-\theta)}{1+\theta}\right]\left[\frac{k\theta}{k\theta+s}\right]}{1-\left[\frac{(1-\theta)}{1+\theta}\right]\left[\frac{k\theta}{k\theta+s}\right]} \quad -(5.6)$$

$$l^*(s) = \frac{2k\theta^2}{[(1+\theta)(k\theta+s)-(1-\theta)k\theta]}$$

$$E(T) = \frac{-dl^*(s)}{ds} \Big/ s=0$$

$$\frac{-d}{ds}\left[\frac{2k\theta^2}{[(1+\theta)(k\theta+s)-(1-\theta)k\theta]}\right] \Big/ s=0$$

$$=-2k\theta^2\left\{-[(1+\theta)(k\theta+s)-(1-\theta)k\theta]^{-2}\right\}(1+\theta)(1)$$

$$= \left[\frac{2k\theta^2(1+\theta)}{[(1+\theta)(k\theta+s)-(1-\theta)k\theta]^2}\right]$$

$$/\, E(T) = \left[\frac{2k\theta^2(1+\theta)}{[(1+\theta)(k\theta+s)-(1-\theta)k\theta]^2}\right] \Big/ s=0$$

$$= \left[\frac{2k\theta^2(1+\theta)}{[(1+\theta)(k\theta)-(1-\theta)k\theta]^2}\right]$$

$$= \frac{2k\theta^2(1+\theta)}{K^2\theta^2(2\theta)^2}$$

$$E(T^2) = \frac{-d}{ds}\left[\frac{-2k\theta^2(1+\theta)}{[(1+\theta)(k\theta+s)-(1-\theta)k\theta]}\right] \Big/ S=0$$

$$= 4k\theta^2(1+\theta)^2[(1+\theta)(k\theta+s)-(1-\theta)k\theta]^{-3} \Big/ s=0$$

$$= \frac{1}{2}\frac{(1+\theta)}{K\theta^2} \quad \text{(On simplification)}$$

$$V(T) = E(T^2) - E(T))^2$$

$$= \frac{1}{2}\frac{(1+\theta)^2}{K^2\theta^4} - \left[\frac{1}{2}\frac{(1+\theta)}{K\theta^2}\right]^2$$

$$= \frac{1}{4}\left[\frac{2(1+\theta)^2-(1+\theta)^2}{k^2\theta^4}\right]$$

$$= \frac{1}{4}\frac{(1+\theta)^2}{k^2\theta^4}$$

$$= \frac{}{=}\left[\frac{1}{2}\frac{(1+\theta)}{K\theta^2}\right]^2 > 0$$

Numerical Illustration

Table 5. 1

θ = 0. 5		
K	E(T)	V(T)
1	3. 0000	9. 0000
2	1. 5000	2. 2500
3	1. 0000	1. 0000
4	0. 7500	0. 5625
5	0. 6000	0. 3600

6	0. 5000	0. 2500
7	0. 4286	0. 1837
8	0. 3750	0. 1406
9	0. 3333	0. 1111
10	0. 3000	0. 9000

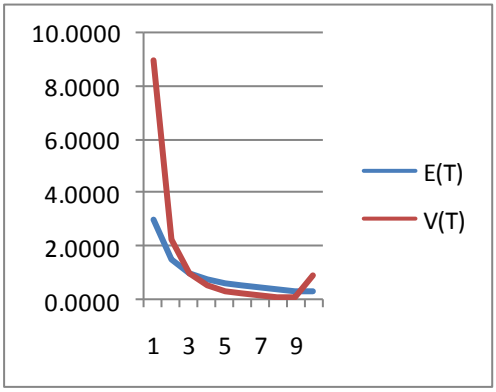
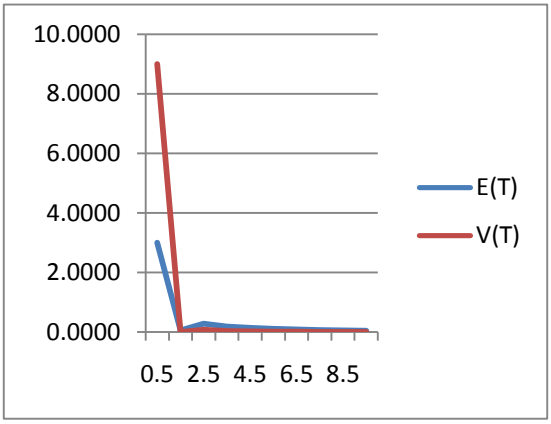


Table 5. 2

K = 1		
θ	**E(T)**	**V(T)**
0. 5	3. 0000	9. 0000
1. 5	0. 0556	0. 0031
2. 5	0. 2800	0. 0784
3. 5	0. 1837	0. 0337
4. 5	0. 1358	0. 0184
5. 5	0. 1074	0. 0115
6. 5	0. 0888	0. 0079
7. 5	0. 0667	0. 0045
8. 5	0. 0588	0. 0035
9. 5	0. 0431	0. 0019



Conclusion

The following conclusions are made on the basis of numerical illustrations.

i. In table 5. 1, the value of the threshold parameter of geometric distribution θ is fixed and the number of contacts in (0, t) namely k increases it means that the contacts are more frequent. In other words the interarrival time between contacts become shorter. Hence it takes less time to cross the threshold. It displayed on the graph 5. 1.
ii. In table 5. 2 the value of the parameter θ which is namely the parameter of the distribution of the interarrival time which is given by $E(U) = 1/\theta$ since $U \sim \exp(\theta)$.

Therefore the interarrival time between contacts becomes smaller and hence mean time to seroconversion decreases. Hence varience of seroconversion also decreases.

References

[1] Esary J. D. Marshall A. W. and Proschan F. Shock models and wear process. Ann. Probability, 1(4): 627-649(1973).
[2] Jewel N. P. and Shiboshi S. statistical analysis of HIV infectivity based on Partner Studies, Biometers. 46, 1133-1150 (1990).
[3] Kannan R. Venkatachalam K. A. Sathiya Moorthi R. and Malarvizhi G. A stochastic approach to determine the expected time to seroconversion of HIV infected. The Journal of Indian Acad. Of Math., 29(1): 237-249(2007).
[4] Kannan. R. Ganesan. A and Sathiyamoorthi. R, A stochastic model for estimation of expected time to seroconversion of HIV infected using order statistics. Bio Science Research Bulletin: 24(1): 41-47.
[5] Nowak, M. A. and May, R. M. Mathematical biology of HIV infections antigenic variation and diversity threshold. Mathematical Biosciences, 106: 1-21 (1991).
[6] Parvathi. s et al stochastic analysis of single product inventory system with sales when both demands and funds are available. International Journal of Mathematical Archive, 4(8)(2013):134-139
[7] Premila, S. C., and Srinivasa Raghavan S. A stochastic model for the estimation of time to seroconversion of HIV transmission using geometric distribution. Applied Mathematical Sciences, 157: 7803-7811 (2014).
[8] Stilianakis, N., Schenzle, D., and Dietz K. On the antigenic diversity threshold model for AIDS. Mathematical Biosciences, 121: 235-247 (1994).